SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed on Form PTO-1449 **(Exhibit A)** and are also listed below.

Reference items 1-15 are either U.S. Patents or U.S. Patent Application Publications. Pursuant to 37 C.F.R. 1.98(a)(2), copies of references 1-15 are not being submitted.

In addition, copies of the documents listed herein as items 24-28 are not provided because these Hungarian Patents correspond to either WIPO publications or European patents, copies of which are included herein already.

Copies of the documents listed herein as items 16-23 and 29-128 are attached hereto as **Exhibits 1-108.**

1. U.S. Patent No. 5,296,484, issued March 22, 1994, Coghlan, M. J. et al.;

2. U.S. Patent No. 5,646,130, issued July 8, 1997, Shi, G. H.;

3. U.S. Patent No. 5,877,180, issued March 2, 1999, Linden et al.;

4. U.S. Patent No. 5,889,026, issued March 30, 1999, Alanine et al.;

5. U.S. Patent No. 5,935,964, issued August 10, 1999, Baraldi et al.;

6. U.S. Patent No. 6,117,878, issued September 12, 2000 to Linden, J.;

7. U.S. Patent No. 6,465,456, issued October 15, 2002, Springer et al.;

8. U.S. Patent No. 6,916,804, issued July 12, 2005 to Castelhano, A. et al.;

9. U.S. Patent No. 7,202,252, issued April 10, 2007, Wilson et al.;

10. U.S. Patent Application Publication No. 2003-0139427 A1, published November 1, 2005 (Castelhano, A. et al.);

11. U.S. Patent Application Publication No. 2003-0029067-A1, published 12/11/2003 (Castelhano, A. et al.);

12. U.S. Patent Application Publication No. 2005-0119271 A1, published June 2, 2005 (Castelhano, A. et al.);

13. U.S. Patent Application Publication No. 2004-0082599-A1, published 4/29/2004 (Castelhano, A. et al.);

14. U.S. Patent Application Publication No. 2005-0043332 A1, published 2/24/2005 (Castelhano, A. et al.);

15. U.S. Patent Application Publication No. 2008-0070936,

published March 20, 2008 (Castelhano, A. et al.);

16. PCT International Application No. WO 97/47601, published December 18, 1997 **(Exhibit 1)**;

17. PCT International Application No. WO 99/64407, published December 16, 1999 **(Exhibit 2)**;

18. PCT International Application No. WO 99/08460, published February 18, 1999 **(Exhibit 3)**;

19. PCT International Application No. WO 00/03741, published January 27, 2000 **(Exhibit 4)**;

20. PCT International Application No. WO 2003/053361, published July 3, 2003 **(Exhibit 5)**;

21. PCT International Application No. WO 2003/053366, published July 3, 2003 **(Exhibit 6)**;

22. European Patent Application No. EP 0 729 758 A2, published September 4, 1996 **(Exhibit 7)**;

23. European Patent No. EP 1246623 B1, published August 9, 2006 **(Exhibit 8)**;

24. Hungarian Patent No. HU P9303515 (corresponds to WO 94/13676);

25. Hungarian Patent No. HU P9501230 (corresponds to EP 0682027);

26. Hungarian Patent No. HU P9602016 (corresponds to WO 95/19970);

27. Hungarian Patent No. HU P9402829 (corresponds to WO 93/20078);

28. Hungarian Patent No. HU P9602017 (corresponds to WO 95/19774);

29. Abbracchio M., et al., (1997) "Modulation of Apoptosis by Nervous System: a Possible Role for the A_3 Receptor", Ann. NY. Acad. Sci., 825: 11-22 **(Exhibit 9)**;

30. Aoyama S. et al. (2000) "Rescue of Locomotor Impairment in Dopamine D2 Receptor-Deficient Mice by an Adenosine A2a Receptor Antagonist" J. Neuroscience 20(15):5848-5852 **(Exhibit 10)**;

31. Avila, M.Y. (2001) "A1-A2a and A3-Subtype Adenosine receptors Modulate Intraocular Pressure in the Mouse" J. of Pharmacol. 241-245 **(Exhibit 11)**;

32. Baraldi, P.G. et al. (1996) "Pyrazolo [4,3-e]-1,2,4 triazolo [1,5-c]pyrimidine Derivatives: Potent and Selective A2a Adenosine Antagonists" J. Med. Chem. 39:1164-1171 **(Exhibit 12)**;

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35. Baraldi, P.G. et al., (1999) "A1 and A3 adenosine receptor agonists: an overview." *Expert Opinion on Therapeutic Patents*, 9(5):515-527 **(Exhibit 15)**;

36. Baraldi, P.G. et al., (2004) "Allosteric modulators for the A1 adenosine receptor." *Expert Opinion on Therapeutic Patents*, 14(1):71-79 **(Exhibit 16)**;

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41. Bradford M. M., (1976) "A Rapid and Sensitive Method for

the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding", Anal. Biochem., 72: 248 **(Exhibit 21)**;

42. Bremer et al. (2002) "Therapy of Crohn's Disease in Childhood", Expert Opin. Pharmacother. 3(7): 809-825 **(Exhibit 22)**;

43. Broach, J. R., et al., (1983) "Vectors for high level, inducible expression of cloned genes in yeast", Inouye (ed)., Experimental Manipulation of Gene Expression. Academic Press, New York, 83-117 **(Exhibit 23)**;

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48. Coney, A.M. et al. (1998) "Role of Adenosine and its Receptors in the Vasodilation Induced in the Cerebral Cortex of the Rat by Systemic Hypoxia" J. Physiol. 509:507-518 **(Exhibit 28)**;

49. Cooper, J.A. (1995) "Adenosine Receptor-induced Cyclic AMP Generation and Inhibtion of 5-hydroxytryptamine release in Human Platelets" Br. J. Clin. Pharmacol. 40:43-50 **(Exhibit 29)**;

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51. Dubey, R.K. et al. (2001), "A_{2B} Receptors Mediate the Antimitogenic Effects of Adenosine in Cardiac Fibroblasts", Hypertension 37: 716-721 **(Exhibit 31)**;

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59. Franco M., et al., (1999) "Adenosine Regulates Renal Nitric Oxide Production in Hypothyroid Rats", Journal of the American Society of Nephrology, 1681-1688 **(Exhibit 39)**;

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69. Hoeschst India Ltd., India "Pharmacologically active pyrimido "[4,5-b]indoles and their salts." Database accession No. 106:84629 HCA XP002121648 **(Exhibit 49)**;

70. Kanda, T. et al. (1998) "Adenosine A2a Receptors Modify Motor Function in MPTP-treated Common Marmosets" Neuroreport 9:2857-2860 **(Exhibit 50)**;

71. Kanda, T. et al. (2000) "Combined Use of the Adenosine A2a Antagonist KW-6002 with L-DOPA or with Selective D1 or D2 Dopamine Agonists Incrases Antiparkinsonian Activity but not Dyskensia in MPTP-Treated Monkeys" Experimental Neurology 162:321-327 **(Exhibit 51)**;

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73. Kiichiro, K. et al. "Synthesis of pyrazinecarboxylic acid derivs. - (II) derivs. of 3-aminopyrazinecarboxylic acid" Chem. Abstracts 56:8713, Chemical Abstracts Service, Columbus Ohio, US XP 002121649 **(Exhibit 53)**;

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76. Knutsen, L.J.S. et al. (2001) Curr. Opin. Invest. Drugs 2(5):668-673 **(Exhibit 56)**;

77. Kopf, S.R. et al. (1999) "Adenosine and Memory Storage: Effect of A1 and A2 Receptor Antagonists" Psychopharmacology 146:214-219 **(Exhibit 57)**;

78. Li, J.M. et al. (1998) "Adenosine A2a Receptors Incrase Arterial Endothelial Cell Nitric Oxide" J. Surg. Res. 80:357-364 **(Exhibit 58)**;

79. Linden, J. et al., (1998) "The Structure and Function of A1 and A2B Adenosine Receptors" Life Sciences 62(17-18): 1519-1524 **(Exhibit 59)**;

80. Meade et al., PubMed Abstract (Life Sci. 69(11):1225-40) August 2001 **(Exhibit 60)**;

81. Mitchell, C.H. et al., "Adenosine A3 Receptor Activation Reduces Cell Volume and Activates Cl^- Current in Human Ciliary Epithelial Cells", *FASEB J*, A134 (Abstract only) **(Exhibit 61)**;

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84. Montesinos, M.C. et al. (2002) "Adenosine Promotes Wounds Healings and Mediates Angiogenesis in Response to Tissue Injury Via Occupancy of A2a Receptors" American Journal of Pathology 160(6):2009-2018 **(Exhibit 64);**

85. Müller, C.E. et al., (2002) J. Med. Chem. 45(16): 3440-3450 **(Exhibit 65);**

86. Müller, C.E. (2001) "A_3 Adenosine Receptor Antagonists" Mini Reviews in Med. Chem. 1(4): 339 **(Exhibit 66);**

87. Nagarathnam, D. et al., (1998) "Design and Synthesis of Novel α1a Adrenoceptor-Selective Dihydropyridine Antagonists for the Treatment of Benign Prostatic Hyperplasia", J. Med. Chem. 41(26): 5320-5333 **(Exhibit 67);**

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89. Ohana G., et al., (2001) "Differential Effect of Adenosine on Tumor and Normal Cell Growth: Focus on the A3 Adenosine Receptor", Journal of Cellular Physiology, 186: 19-23 **(Exhibit 69);**

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96. Reshkin J., et al., (2000) "Activation of A3 Adenosine Receptor Induces Calcium Entry and Chloride Secretion in A6 Cells", J. Membrane Biol., 178: 103-113 **(Exhibit 76)**;

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99. Shiozaki, S. et al. (1999) "Actions of Adenosine A2a Receptor Antagonist KW-6002 on Drug-induced Catalepsy and hypokinesia Caused by Reserpine of MPTP" Psychopharmacology 147:90-95 **(Exhibit 79)**;

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101. Singh et al., "Immune therapy in inflammatory bowel disease and models of colitis", British Journal of Surgery, 88: 1558-1569, 2001 **(Exhibit 81)**;

102. Strohmeier, G. R. et al., (1995) "The A_{2b} Adenosine Receptor Mediates cAMP Responses to Adenosine Receptor Agonists in Human Intestinal Epithelia", J. Bio. Chem., 270: 2387-2394 **(Exhibit 82)**;

103. Svenningsson, P. et al. (1999) "Distribution, Biochemistry and Function of Striatal Adenosien A2a Receptors" Prog. Neurobiol. 59(4):355-396 **(Exhibit 83)**;

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(Exhibit 84);

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106. Van Niel, M.B. et al., "Fluorianation of 3-(3-(Piperidin-1-yl)propyl)indoles and 3-(3-(Piperazin-1-yl)propyl) indoles Gives Selective Human 5-Htid Receptor Ligands with Improved Pharmokinetic Profiles" J. Med. Chem. (1999) 42(12): 2087-2104 **(Exhibit 86);**

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108. Von Lubitz D., et al., (1999) "Stimulation of Adenosine A3 Receptors in Cerebral Ischemia", Ann. NY. Acad. Sci., 890: 93-106 **(Exhibit 88);**

109. Von Lubitz, D., et al., (1999) "Chronic administration of adenosine A3 receptor agonist and cerebral ischemia: neuronal and glial effects", European Journal of Pharmacology, 367: 157-163 **(Exhibit 89);**

110. West, R.A. et al. (1961) "2-alkyl(aryl)-and 2,7-dimethyl-4-substituted aminopyrrolo[2,3–d]pyrimidines." *J. Org. Chem.*, 26:3809-3812 **(Exhibit 90);**

111. Yan, Luo et al. (2003) Expert Opinion on Emerging Drugs,

vol. 8, no. 2 pp. 537-576 **(Exhibit 91)**;

112. Yao Y., et al., (1997) "Adenosine A3 Receptor Agonists Protect HL-60 and U-937 Cells from Apoptosis Induced by A3 Antagonists", Biochemical And Biophysical Research Communications, 232: 317-322 **(Exhibit 92)**;

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114. International Search Report issued in PCT International Application No. PCT/US99/12135, filed June 1, 1999 **(Exhibit 94)**;

115. International Search Report issued in PCT International Application No. PCT/US00/32702, filed December 1, 2000 **(Exhibit 95)**;

116. International Search Report issued in PCT International Application No. PCT/US2001/045280, filed November 30, 2001 **(Exhibit 96)**;

117. International Search Report issued in PCT International Application No. PCT/US2002/38055, filed November 27, 2002 **(Exhibit 97)**;

118. International Search Report issued in PCT International Application No. PCT/US2002/40890, filed December 20, 2002 **(Exhibit 98)**;

119. International Search Report issued in PCT International Application No. PCT/US2002/41273, filed December 20, 2002 **(Exhibit 99)**;

120. PCT International Preliminary Examination Report issued in PCT International Application No. PCT/US99/12135 **(Exhibit 100)**;

121. PCT International Preliminary Examination Report issued in PCT International Application No. PCT/US00/32702 **(Exhibit 101)**;

122. PCT International Preliminary Examination Report issued in PCT International Application No. PCT/US2001/045280, filed November 30, 2001 **(Exhibit 102)**;

123. PCT International Preliminary Examination Report issued in PCT International Application No. PCT/US2002/38055, filed November 27, 2002 **(Exhibit 103)**;

124. PCT International Preliminary Examination Report issued in PCT International Application No. PCT/US2002/40890, filed December 20, 2002 **(Exhibit 104)**;

125. PCT International Preliminary Examination Report issued in PCT International Application No. PCT/US2002/41273, filed December 20, 2002 **(Exhibit 105)**;

126. Supplemental European Search Report; for EP Application No. 02 80 5676; issued 2/7/2005 **(Exhibit 106)**;

127. Partial European Search Report for EP Application No. 06 01 6543.8; completed 10/4/2006 **(Exhibit 107)**; and

128. Partial European Search Report; for EP Application No. 01 99 7029; completed 12/21/2004 **(Exhibit 108)**.

Applicants request that the Examiner review the references and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $120.00 fee for a one-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any other fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Gary J. Gershik 5/9/08

John P. White Date
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EXHIBIT A
Applicants: Arlindo Castelhano et al.
Application No.: 10/718,280
Filed: November 20, 2003